ORIGINAL ARTICLE

Myasthenia gravis in adults of institutions pertaining to the Mexican public health system: an analysis of hospital discharges during 2010

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Abstract

Introduction: *Epidemiological studies on MG in Mexico are mainly derived from experiences in referral centers.* **Objective:** *To describe the epidemiological characteristics of hospital discharges during the year 2010 with the diagnosis of MG in adults admitted in hospitals of the Mexican public healthcare system.* **Methods:** *The 2010 hospital discharges database of the SINAIS (Secretaría de Salud, Instituto Mexicano del Seguro Social [IMSS], IMSS Oportunidades, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado [ISSSTE], PEMEX, SEMAR and SEDENA) was reviewed. MG records were identified by the G70.0 code of the International Classification of Diseases, 10th revision (ICD-10).* **Results:** *During 2010, 5,314,132 hospital discharges were recorded (4,254,312 adults), out of which 587 (0.001%) were adults with MG (median age: 47 years; 60% females). Women with MG were significantly younger than men (median age: 37 vs. 54 years, respectively; $p < 0.001$). Median hospital stay was 6 days. Hospital mortality rate was 3.4%, without differences by gender. Age was associated with the probability of death.* **Conclusions:** *Gender-associated bimodal distribution of age was substantiated. Hospital mortality rate in Mexico is consistent with recent reports around the world.* (Gac Med Mex. 2015;151:43-9)

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KEY WORDS: *Age. Epidemiology. Hospitalization. MG. Mexico. Mortality.*

Introduction

Myasthenia gravis (MG) is an autoimmune disease of the neuromuscular junction characterized by fluctuating muscular weakness that worsens with physical activity and affects specific muscle groups[1-3]. The prevalence of MG approaches 20 cases per each 100,000 inhabitants in the U.S.A. and has shown an increase in the last decades, probably due to treatment improvement and increased survival of these patients[4,5]. Heterogeneity of the data reported in studies makes it difficult estimating a generalizable incidence; however, figures between 1.7 and 21.3 cases per each million of persons per year are reported[6]. The influence of age and sex on presentation rates has shown consistent associations. Incidence increases with age, but in women there is an important peak before 40 years

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of age, whereas in people older than 50, incidence is predominant in men[7]. In Asia, up to 50% of MG cases occur in children[8].

About 50 years ago, MG mortality was between 50 and 80% of cases, but it has been decreasing thanks to treatment advances and, recently, mortality is reported to range from 5 to 10% around the world[9-11].

In Mexico, epidemiological information on MG is very limited in terms of frequency, mortality and other demographic characteristics. There are Mexican studies trying to answer these questions, but neither of them has a national approach. This represents a difficulty in the design of new descriptive and interventional trials that allow for the care of MG patients to be improved in our country.

Methods

In the present observational study, the 2010 hospital discharges database of institutions pertaining to the Mexican public healthcare system, made available by the National Health Information System (SINAIS; available at http://www.sinais.salud.gob.mx[12]) was reviewed. In this analysis, hospitals of the Ministry of Health (Secretaría de Salud), were included (including National Institutes, such as IMSS, IMSS Oportunidades, ISSSTE, PEMEX, SEMAR, SEDENA and Seguro Popular). Information on the period corresponding to year 2010 hospital discharges reported in adults was extracted and analyzed. MG records were electronically identified using ICD-10 codes (G70.0 code). Only the final discharge diagnosis was considered and selected for this analysis. Patients aged < 18 years were excluded, as well as cases without information on admission and discharge date or without complete essential demographic data, such as age, gender and place of residence. One by one, the record numbers, institutional codes, demographic data and ID numbers were reviewed in order to avoid repeated inclusion of patients who received care for the same diagnosis on more than one occasion during the analyzed period. In case a patient was identified with several discharges recorded during 2010, the last discharge of the year was considered for the analysis, eliminating previous records.

Nominal variables were presented as simple relative frequencies. Since age and days of hospital stay did not show a normal distribution, medians with interquartile range (IQR, or 25 and 75 percentiles) were used to express central tendency measures. Pearson's chi-square test was used to compare the frequencies of

qualitative nominal variables between two groups or to assess homogeneity in the distribution of these variables in 3 or more groups. Student t-test was used in the comparison of normally distributed quantitative variables, and the Mann-Whitney U-test, in the comparison of non-parametric distribution quantitative variables, both for two independent groups. The hospital case fatality rate was provided. Hospital length of stay and mortality were standardized to a 30-day assessment. That is, patients who remained hospitalized > 30 days and died in the hospital after this time limit were considered to be alive until day 30. Thus, for the survival analysis, the standardized 30-day hospital mortality rate was reported, with actuarial analyses graphs constructed using the Kaplan-Meier method to assess the probability of survival during hospitalization according to age and gender. Mortality differences in the actuarial analyses were compared with the log-rank test. Alpha error (p-value) was two-tailed and considered to be significant when $p < 0.05$. The SPSS statistical pack v. 20.0 was used for all calculations.

Results

During 2010, 5,314,132 hospital discharges were recorded in the Mexican public healthcare system (4,254,312 adult discharges), out of which, a total of 587 (0.01%) were discharges associated with an MG diagnosis in adults (median age: 47 years; IQR: 30 to 61 years; 60% females, 40% males). Most hospital discharges with a MG diagnosis were from states with referral centers (often tertiary care hospitals) (Table 1).

As expected, a gender-associated bimodal frequency of age was observed, in such a way that the age of women was significantly lower than in men (median age: 37 vs. 54 years, respectively; $p < 0.001$) (Fig 1). Thus, the highest proportion of female cases was in the group under 40 years of age, whereas in the group of patients older than 50 years, male gender was characteristic.

Mean hospital stay was 9.08 days (median: 6 days, IQR: 3 to 10 days). A total of 20 (3.4%) MG-associated hospital deaths were recorded during 2010. No gender differences were observed with regard to case fatality rate (mortality in men: 3.4%; in women: 3.4%; $p = 0.99$) or hospital length of stay (median stay in men: 6 days; in women: 6 days; $p = 0.76$). Old age was associated with a higher likelihood of in-hospital mortality (Figs. 2 and 3). Correspondingly, both age (median: 63.5 vs. 47 years: $p = 0.04$) and hospital

Table 1. Relative frequency of cases discharged with a MG diagnosis in public hospitals of the Mexican healthcare system, by State

| State	Gender		Deaths		Total (n = 587)
	Male (n = 235)	Female (n = 352)	No (n = 567)	Yes (n = 20)	
Aguascalientes, n (%)	0	1 (0.3)	1 (0.2)	0	1 (0.2)
Baja California, n (%)	10 (4.3)	9 (2.6)	17 (3.0)	2 (10.0)	19 (3.2)
Baja California Sur, n (%)	0	2 (0.6)	2 (0.4)	0	2 (0.3)
Campeche, n (%)	0	0	0	0	0
Coahuila, n (%)	5 (2.1)	15 (4.3)	20 (3.5)	0	20 (3.4)
Colima, n (%)	0	1 (0.3)	1 (0.2)	0	1 (0.2)
Chiapas, n (%)	0	3 (0.9)	2 (0.4)	1 (5.0)	3 (0.5)
Chihuahua, n (%)	5 (2.1)	6 (1.7)	11 (1.9)	0	11 (1.9)
Distrito Federal, n (%)	58 (24.7)	117 (33.2)	173 (3.5)	2 (10.0)	175 (29.8)
Durango, n (%)	4 (1.7)	1 (0.4)	10 (1.8)	0	10 (1.7)
Guanajuato, n (%)	8 (3.4)	9 (2.6)	15 (2.6)	2 (10.0)	17 (2.9)
Guerrero, n (%)	1 (0.4)	1 (0.3)	2 (0.4)	0	2 (0.3)
Hidalgo, n (%)	1 (0.4)	2 (0.6)	3 (0.5)	0	3 (0.5)
Jalisco, n (%)	26 (11.1)	30 (8.5)	54 (9.5)	2 (10.0)	56 (9.5)
Estado de México, n (%)	5 (2.1)	5 (1.4)	9 (1.6)	1 (5.0)	10 (1.7)
Michoacán, n (%)	8 (3.4)	5 (1.4)	13 (2.3)	0	13 (2.2)
Morelos, n (%)	1 (0.4)	6 (1.7)	6 (1.1)	1 (5.0)	7 (1.2)
Nayarit, n (%)	1 (0.4)	2 (0.6)	3 (0.5)	0	3 (0.5)
Nuevo León, n (%)	34 (14.6)	36 (10.2)	70 (12.3)	0	70 (11.9)
Oaxaca, n (%)	3 (1.3)	5 (1.4)	8 (1.4)	0	8 (1.4)
Puebla, n (%)	7 (3.0)	15 (4.3)	21 (3.7)	1 (5.0)	22 (3.7)
Querétaro, n (%)	0	0	0	0	0
Quintana Roo, n (%)	0	6 (1.7)	5 (0.9)	1 (5.0)	6 (1.0)
San Luis Potosí, n (%)	5 (2.1)	2 (0.6)	7 (1.2)	0	7 (1.2)
Sinaloa, n (%)	9 (3.8)	8 (2.3)	16 (2.8)	1 (5.0)	17 (2.9)
Sonora, n (%)	7 (3.0)	23 (6.5)	29 (5.1)	1 (5.0)	30 (5.1)
Tabasco, n (%)	2 (0.9)	4 (1.1)	6 (1.1)	0	6 (1.0)
Tamaulipas, n (%)	9 (3.8)	5 (1.4)	13 (2.3)	1 (5.0)	14 (2.4)
Tlaxcala, n (%)	1 (0.4)	1 (0.3)	2 (0.4)	0	2 (0.3)
Veracruz, n (%)	14 (6.0)	10 (2.8)	21 (3.7)	3 (15.0)	24 (4.1)
Yucatán, n (%)	8 (3.4)	14 (4.0)	21 (3.7)	1 (5.0)	22 (3.7)
Zacatecas, n (%)	3 (1.3)	3 (0.9)	6 (1.1)	0	6 (1.0)
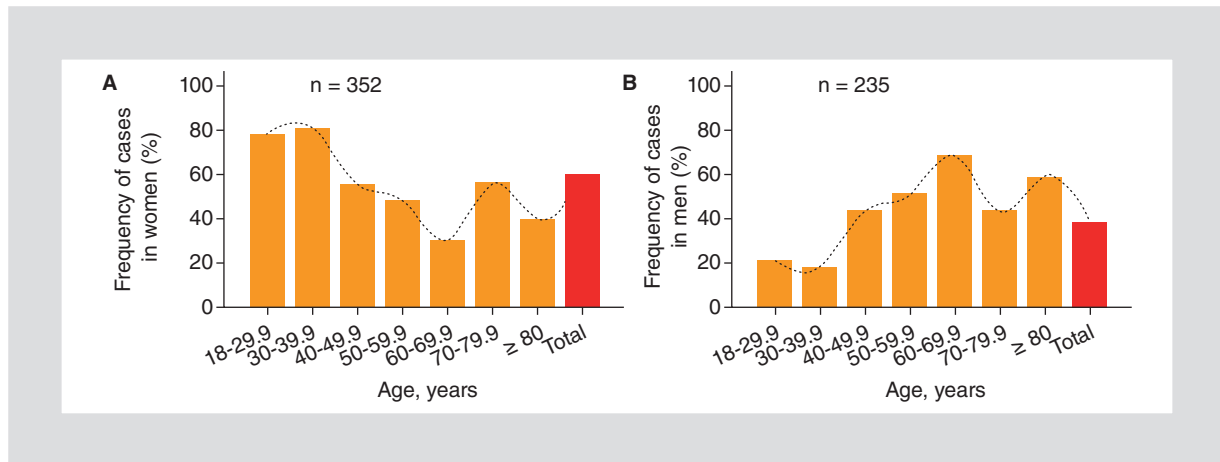
Figure 1. *Relative frequency of discharge cases with a MG diagnosis in the Mexican public healthcare system during the year 2010 (n = 587). A: frequency of diagnoses in the female gender. B: frequency of diagnoses in the male gender.*
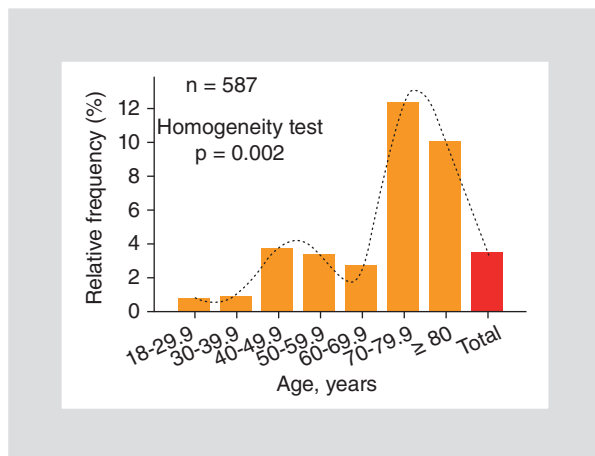

Figure 2. *MG diagnosis-associated hospital case fatality rate in patients hospitalized during the year 2010, by age group.*

length of stay (median: 12.5 vs. 6 days; p = 0.02) were significantly higher in the group of death cases, compared to survivors. No more than 3 MG discharge diagnosis-associated fatalities were reported by each State. The states reporting higher relative hospital mortality rates were Chiapas, Quintana Roo and Morelos (Fig. 4).

Discussion

The percentage of MG cases in women was 60%, similar to that reported by Echeverría-Galingo et al. in western Mexico[13], and lower than the 78 and 88% figures observed by Navarro-Reynoso et al. and Remes-Troche et al., respectively[14,15]. Both these last
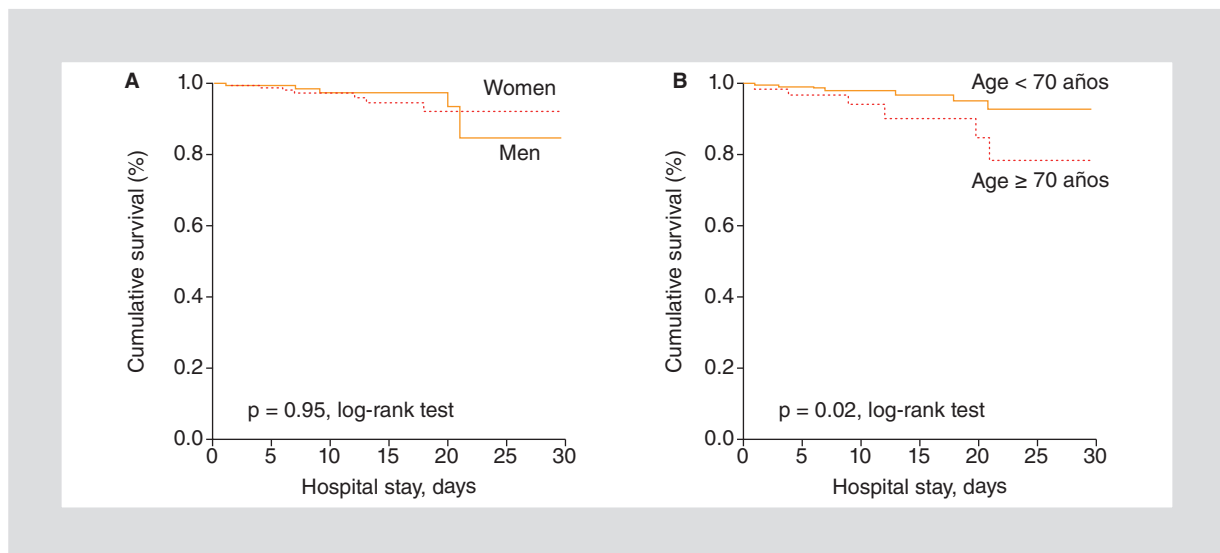

Figure 3. *Actuarial analysis with the Kaplan-Meier method. A: 30-day standardized hospital mortalty by gender. B: 30-day standardized hospital mortalty by age.*
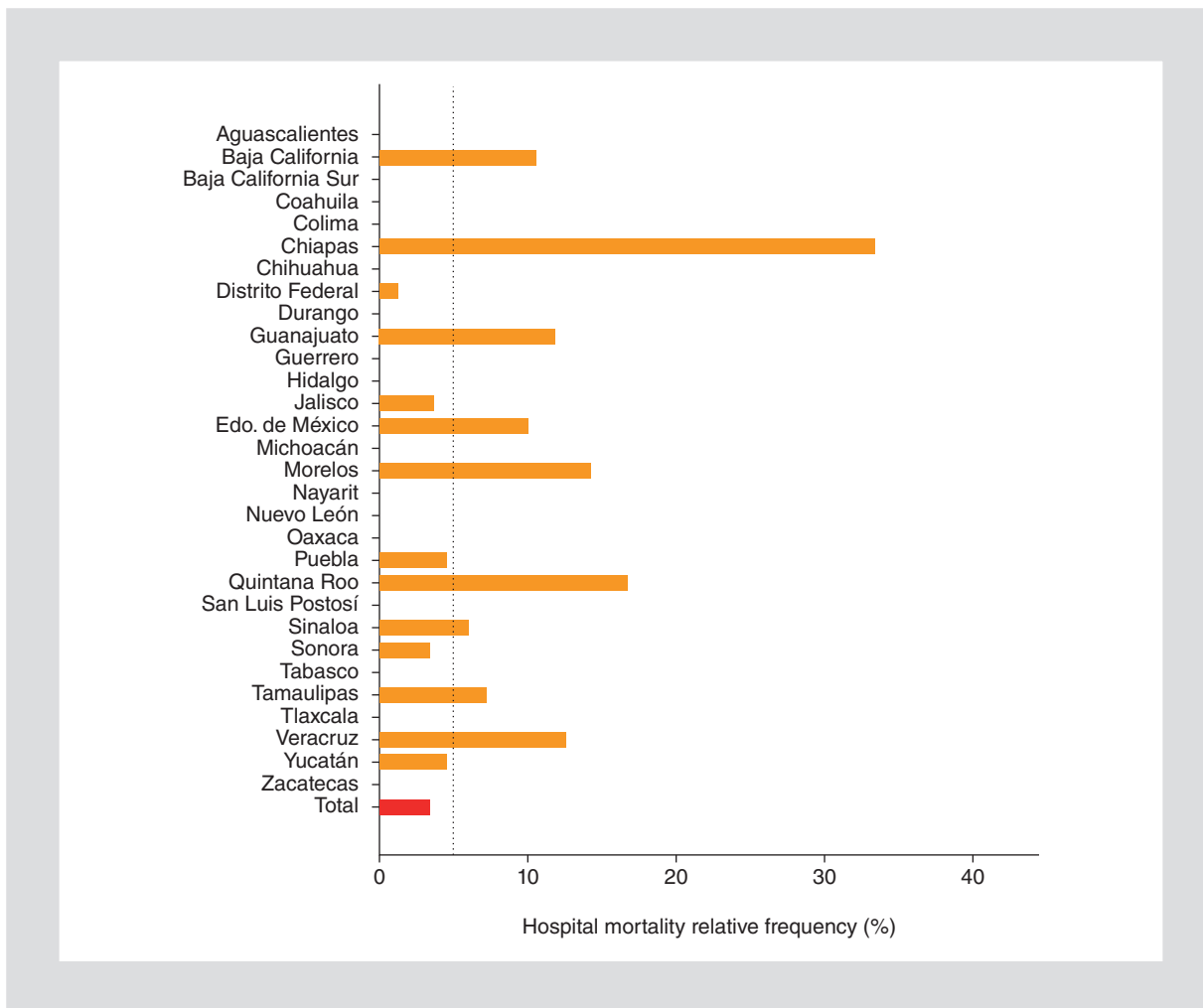
Figure 4. *MG diagnosis-associated hospital mortality in hospitalized patients during the year 2010, by State.*

results were obtained in referral hospitals in Mexico City, which may contribute to this difference in gender distribution. Our results are consistent with the gender-associated bimodal presentation reported in other studies[4,16,17], with higher proprtions of women in the younger than 40-year age-group and men in the group older than 50 years.

In an epidemiological study from the U.S.A., which included 5,502 patients, a 2.2% hospital case fatality rate was observed in MG-diagnosed inpatients, which increased to 4.4% when they were admitted due to myasthenic crisis[18]. The authors concluded that the respective hospital mortality rates were low compared to other reports. With regard to our analysis, it is important pointing out that in the ICD-10 system, myasthenic crisis has no specific classification assigned and, therefore, it can be inferred that most hospitalization cases with a MG diagnosis might be due to crisis

or decompensation that required hospital admission. Additionally, finding out the direct cause of death was not possible, except when it was associated with MG being recorded of as the main diagnosis. Therefore, taking into account that myasthenic crisis reported mortality ranges from 5 to 10%[19-18], the 3.4% rate found in the present analysis can be regarded as being low compared to traditional reports, but similar to findings described in contemporary studies for the North American population.

Factors associated with death (not necessarily its cause) were longer hospital stay and age. The relationship with age has been reproduced in numerous studies. Alshekhlee et al. reported that mortality increase was constant for each decade and that age was one of the main predictors of death[18], whereas Christensen et al. documented that, after 50 years, mortality increased and that, after 60, the increase in mortality was

greater[19]. On the other hand, mean hospital length of stay reported in a study conducted by Souayah et al. in the U.S.A. was 22 days, markedly longer than that found in the present study (9 days, with a median of 6)[20], but if we take into account the study published by Alshekhlee et al., where average length of stay was 4 days for MG diagnosis and 6 for myasthenic crisis, our hospital length of stay would be, in fact, somewhat longer. In some studies on general mortality in intensive care units, where a group of conditions including MG are assessed, a relationship is established between a long hospital stay and greater mortality[21]. Conversely, most studies refer to respiratory failure or ventilatory support requirement as the most important mortality-associated factor. Kiphuth et al. suggest that mechanic ventilation duration is better predictor of an adverse outcome than hospital length of stay, since patients on mechanic ventilation necessarily are hospitalized, but not all hospitalized patients require mechanical ventilation[22]. The results observed in the present study with regard to hospital length of stay are likely due, in part, to this phenomenon.

The main limitation of the study is that its results should be regarded as exploratory, since the diagnoses here considered were made within the health institutions, without any validation by an expert committee. Additionally, the frequency of reported cases by state does not necessarily reflect the incidence or prevalence of the region, since many patients are treated outside their place of residence. Big cities tend to concentrate the highest proportion of cases. Furthermore, hospital case fatality rate does not necessarily reflect healthcare institutions capacity to solve health problems, since in some states there are referral centers that absorb the most complicated cases. In spite of these limitations, descriptive explorations as the one here presented offer useful data for the design of new observational and interventional studies, which will allow for this condition to be better understood in order to offer better care to patients who suffer it. The usefulness of this type of analysis of information provided by the Mexican public healthcare system has already been previously established[23-28], as well as the importance of having this kind of information, which is essential to establish effective health programs, has been recognized[29].

Conclusion

The information obtained through the analysis of discharges from the Mexican healthcare system is consistent with current literature. The frequency of MG increases with age. There is a larger proportion of female cases before 40 years of age and, in males, the proportion is greater after 50 years. Mortality is 3.4%, slightly lower than previously reported figures. Main mortality-associated factors were age and number of hospital-stay days. These results allow for a general outlook on MG epidemiology in Mexico and the health burden this condition represents to be obtained. It is a base that invites for more multi-center, national-wide studies to be carried out, in order to explore a larger number of variables and enable a more comprehensive characterization of MG.

Conflicts of interest

The authors declare there are no potential conflicts of interest relevant to the subject matter discussed in this contribution.

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